

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	("6949584").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:01
L2	438	(514/475).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:02
L3	6	TNP-470 adj conjugate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:10
L4	11	Ronit.inv. and Satchi.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:12
L5	120	Judah.inv. and Folkman.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:11
L6	11	Ronit.inv. and Satchi.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:12

EAST Search History

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L1	2	("6949584").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:01
L2	438	(514/475).CCLS.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:02
L3	6	TNP-470 adj conjugate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:10
L4	11	Ronit.inv. and Satchi.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:12
L5	120	Judah.inv. and Folkman.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:11
L6	11	Ronit.inv. and Satchi.inv.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/10/02 16:12

10/511,009

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NEWS 19 SEP 21 CA/CAplus fields enhanced with simultaneous left and right
truncation
NEWS 20 SEP 25 CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 21 SEP 25 CAS REGISTRY(SM) no longer includes Concord 3D coordinates
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MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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10/511,009

DN 145:180960
TI Method for monitoring early treatment response
IN Norfray, Joseph F.
PA Receptomon, LLC, USA
SO U.S. Pat. Appl. Publ., 12pp., Cont.-in-part of U.S. Ser. No. 53,059.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | US 2006177378 | A1 | 20060810 | US 2005-193037 | 20050729 |
| | US 2006177377 | A1 | 20060810 | US 2005-53059 | 20050208 |
| | WO 2006086159 | A2 | 20060817 | WO 2006-US2675 | 20060126 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
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VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRAI US 2005-53059 A2 20050208
US 2005-193037 A 20050729

AB Disclosed is a method for monitoring early treatment response of a cancer treatment comprising measuring by magnetic resonance spectroscopy (MRS), for example, proton MRS, the amount of Choline present in the tissue adjoining or surrounding the cancerous tissue before and after treatment; the treatment comprises administration of an angiogenesis inhibitor, for example, a VEGF inhibitor, whereby a decrease in the amount of Choline after treatment is indicative of a pos. response. The decrease in the amount of Choline represents the decrease in the internal cell membrane as a result of down regulation of the organelles and their secretory granules and their transport vesicles. Disclosed also is a method for determining effectiveness of an angiogenesis inhibitor in the treatment of cancer. Also disclosed are methods of monitoring early treatment response in diseases where an angiogenesis effector, i.e., an inhibitor or promoter of angiogenesis, is employed. Also disclosed is a method for monitoring protein translation related to angiogenesis.

L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:796477 CAPLUS

DN 145:180959

TI Method for monitoring early treatment response

IN Norfray, Joseph F.

PA Receptomon, Llc., USA

SO U.S. Pat. Appl. Publ., 11pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | US 2006177377 | A1 | 20060810 | US 2005-53059 | 20050208 |
| | US 2006177378 | A1 | 20060810 | US 2005-193037 | 20050729 |
| | WO 2006086159 | A2 | 20060817 | WO 2006-US2675 | 20060126 |
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 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
 MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
 SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
 VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

PRAI US 2005-53059 A2 20050208
 US 2005-193037 A 20050729

AB Disclosed is a method for monitoring early treatment response of a cancer treatment comprising measuring by magnetic resonance spectroscopy (MRS), for example, proton MRS, the amount of Choline present in the tissue adjoining or surrounding the cancerous tissue before and after treatment; the treatment comprises administration of an angiogenesis inhibitor, for example, a VEGF inhibitor, whereby a decrease in the amount of Choline after treatment is indicative of a pos. response. The decrease in the amount of Choline represents the decrease in the internal cell membrane as a result of down regulation of the organelles and their secretory granules and their transport vesicles. Disclosed also is a method for determining effectiveness of an angiogenesis inhibitor in the treatment of cancer. Also disclosed are methods of monitoring early treatment response in diseases where an angiogenesis effector, i.e., an inhibitor or promoter of angiogenesis, is employed.

L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:790844 CAPLUS

DN 145:202923

TI Method using an anti-VEGF monoclonal antibody and a HPMA copolymer-TNP-470 conjugate for treatment of angiogenic diseases

IN Folkman, Judah; Satchi-Fainaro, Ronit

PA Children's Medical Center Corporation, USA

SO PCT Int. Appl., 45pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2006084054 | A2 | 20060810 | WO 2006-US3712 | 20060202 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW | | | | |
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IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRAI US 2005-649235P P 20050202

AB The invention discloses methods for treating cancer and angiogenic diseases comprising administering an anti-VEGF (vascular endothelial growth factor) monoclonal antibody (e.g. Avastin) and a N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer-TNP-

10/511,009

470 conjugate (e.g. Caplostatin) to a patient in need thereof. Preparation of HPMA copolymer-TNP-470 conjugate is described.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:736387 CAPLUS
DN 145:180945
TI Lipocalin 2 in reversing epithelial to mesenchymal transition and for treatment or prevention of cancer metastasis, angiogenesis, and fibrosis
IN Sukhatme, Vikas P.; Karumanchi, S. Ananth; Seth, Pankaj; Hanai, Junichi; Mammoto, Tadanori; Barasch, Jonathan; Mori, Kiyoshi
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|----------|
| PI WO 2006078717 | A2 | 20060727 | WO 2006-US1738 | 20060119 |
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PRAI US 2005-645438P P 20050119

AB The invention invention shows lipocalin 2 in reversing epithelial to mesenchymal transition and for treatment or prevention of cancer metastasis, angiogenesis, and fibrosis. Lipocalin 2 suppresses cell invasiveness, blocks VEGF production and induces thrombospondin, thereby inhibiting many of the signaling pathways and processes that contribute to angiogenesis and metastasis.

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:515900 CAPLUS
DN 145:1037
TI Method and composition using agents increasing intracellular accumulation of NADH + H⁺ for enhancing anti-angiogenic therapy
IN Ben-Sasson, Shmuel A.
PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| PI WO 2006056889 | A2 | 20060601 | WO 2005-IB4069 | 20051005 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, | | | | |

SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRAI US 2004-616348P P 20041006

AB The invention relates to the discovery that agents that increase intracellular accumulation of NADH + H⁺ enhance the anticancer effects of angiogenesis inhibitors. Furthermore, treatment of a mammal with a combination of at least one angiogenesis inhibitor and at least one agent that enhances intracellular accumulation of NADH + H⁺ allows for the enhanced treatment and/or prevention of angiogenic diseases and disorders.

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1005963 CAPLUS

DN 143:279399

TI antiangiogenic compounds for treating disorders associated with vascular permeability

IN Soker, Shay; Satchi-Fainaro, Ronit

PA USA

SO U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of Appl. No. PCT/US03/11265.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|------|----------|-----------------|----------|
| PI | US 2005203013 | A1 | 20050915 | US 2004-962723 | 20041012 |
| | WO 2003086178 | A2 | 20031023 | WO 2003-US11265 | 20030411 |
| | WO 2003086178 | A3 | 20040108 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-371841P P 20020411

WO 2003-US11265 A2 20030411

AB The invention relates to methods for decreasing or inhibiting disorders associated with vascular hyperpermeability and to methods of screening for compds. that affect permeability, angiogenesis and stabilize tight junctions. In one aspect of the invention there is provided a method of decreasing or inhibiting vascular hyperpermeability in an individual in need of such treatment. The method includes administering to the individual an effective amount of an antiangiogenic compound selected from the group consisting of endostatin, thrombospondin, angiostatin, tumstatin, arrestin, recombinant EPO and polymer conjugated TNP-470. Other antiangiogenic compds. are disclosed herein.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:294991 CAPLUS

DN 143:19427

TI Inhibition of vessel permeability by TNP-470 and its polymer conjugate, caplostatin

AU Satchi-Fainaro, Ronit; Mamluk, Roni; Wang, Ling; Short, Sarah M.; Nagy,

Janice A.; Feng, Dian; Dvorak, Ann M.; Dvorak, Harold F.; Puder, Mark;
 Mukhopadhyay, Debabrata; Folkman, Judah
 CS Vascular Biology Program, Department of Surgery, Children's Hospital
 Boston and Harvard Medical School, Karp Family Research Laboratories,
 Boston, MA, 02115, USA
 SO Cancer Cell (2005), 7(3), 251-261
 CODEN: CCAECI; ISSN: 1535-6108
 PB Cell Press
 DT Journal
 LA English
 AB Angiogenesis inhibitors, such as TNP-470 and the nontoxic HPMA copolymer-TNP-470 (caplostatin), are emerging as a class of anticancer drugs. The authors report that TNP-470 and caplostatin inhibit vascular hyperpermeability of tumor blood vessels as well as that induced in mouse skin by different mediators. Treatment with TNP-470 or angiostatin for 3 days was sufficient to reduce permeability of tumor blood vessels, delayed-type hypersensitivity, and pulmonary edema induced by IL-2. TNP-470 also inhibited VPF/VEGF-induced phosphorylation of VEGFR-2, calcium influx, and RhoA activation in endothelial cells. These results identify an activity of TNP-470, that of inhibiting vessel hyperpermeability. This activity likely contributes to TNP-470's antiangiogenic effect and suggests that caplostatin can be used in the treatment of cancer and inflammation.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:1036851 CAPLUS
 DN 142:696
 TI Synergistic treatment of cancer using immunomers in conjunction with chemotherapeutic agents
 IN Kandimalla, Ekambar R.; Agrawal, Sudhir; Wang, Daqin
 PA Hybridon, Inc., USA
 SO PCT Int. Appl., 106 pp.
 CODEN: PIXXD2
 DT Patent
 LA English

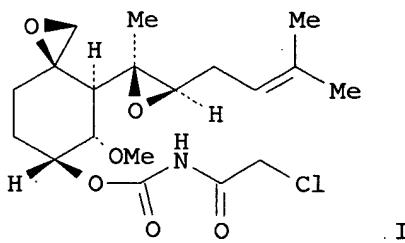
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2004103301 | A2 | 20041202 | WO 2004-US15313 | 20040514 |
| | WO 2004103301 | A3 | 20051103 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
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| | AU 2004241093 | A1 | 20041202 | AU 2004-241093 | 20040514 |
| | CA 2526212 | AA | 20041202 | CA 2004-2526212 | 20040514 |
| | US 2005009773 | A1 | 20050113 | US 2004-846167 | 20040514 |
| | EP 1628531 | A2 | 20060301 | EP 2004-752345 | 20040514 |
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PRAI US 2003-471247P P 20030516
 WO 2004-US15313 W 20040514
 OS MARPAT 142:696
 AB The invention discloses the therapeutic use of immunostimulatory oligonucleotides and/or immunomers in combination with chemotherapeutic agents to provide a synergistic therapeutic effect.
 L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:999688 CAPLUS
 DN 141:428019
 TI TNP-470 species polymer conjugates preparation as angiogenesis inhibitors
 IN Satchi-Fainaro, Ronit; Folkman, Judah
 PA Children's Medical Center Corporation, USA
 SO U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of Appl. No. PCT/US03/10976.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | US 2004229945 | A1 | 20041118 | US 2004-783986 | 20040219 |
| | US 6949584 | B2 | 20050927 | | |
| | WO 2003086382 | A1 | 20031023 | WO 2003-US10976 | 20030410 |
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PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2006020024 | A1 | 20060126 | US 2005-185538 | 20050720 |
| PRAI | US 2002-371791P | P | 20020411 | | |
| | US 2002-414705P | P | 20020930 | | |
| | WO 2003-US10976 | A2 | 20030410 | | |
| | US 2004-783986 | A1 | 20040219 | | |
| OS | MARPAT 141:428019 | | | | |
| GI | | | | | |



AB The present invention relates to conjugates of water-soluble polymers and α -(chloracetyl-carbamoyl) fumagillol (TNP-470) (I) and use of those conjugates as specific intracellular carriers of the TNP-470 into tumor vessels. The present invention further relates to use of those conjugates to lower the neurotoxicity of TNP-470. Most preferably, the polymer has a mol. weight in the range of 15 kDa to 40 kDa. A random copolymer of HPMA and

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methacryloyl-Gly-Phe-Leu-Gly p-nitrophenyl ester was prepared, treated with ethylenediamine linker, and then with I to give the conjugate.

Antitumor and angiogenesis activity of the conjugate were given.

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:161479 CAPLUS
DN 140:368238
TI Targeting angiogenesis with a conjugate of HPMA copolymer and TNP-470
AU Satchi-Fainaro, Ronit; Puder, Mark; Davies, John W.; Tran, Hai T.; Sampson, David A.; Greene, Arin K.; Corfas, Gabriel; Folkman, Judah
CS Vascular Biology Program and Department of Surgery, Boston Children's Hospital and Harvard Medical School, Boston, MA, 02115, USA
SO Nature Medicine (New York, NY, United States) (2004), 10(3), 255-261
CODEN: NAMEFI; ISSN: 1078-8956
PB Nature Publishing Group
DT Journal
LA English
AB Angiogenesis is crucial for tumor growth. Angiogenesis inhibitors, such as O-(chloroacetyl-carbamoyl) fumagillo (TNP-470), are thus emerging as a new class of anticancer drugs. In clin. trials, TNP-470 slowed tumor growth in patients with metastatic cancer. However, at higher doses necessary for tumor regression, many patients experienced neurotoxicity. We therefore synthesized and characterized a water-soluble conjugate of N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer, Gly-Phe-Leu-Gly linker and TNP-470. This conjugate accumulated selectively in tumor vessels because of the enhanced permeability and retention (EPR) effect. HPMA copolymer-TNP-470 substantially enhanced and prolonged the activity of TNP-470 in vivo in tumor and hepatectomy models. Polymer conjugation prevented TNP-470 from crossing the blood-brain barrier (BBB) and decreased its accumulation in normal organs, thereby avoiding drug-related toxicities. Treatment with TNP-470 caused weight loss and neurotoxic effects in mice, whereas treatment with the conjugate did not. This new approach for targeting angiogenesis inhibitors specifically to the tumor vasculature may provide a new strategy for the rational design of cancer therapies.

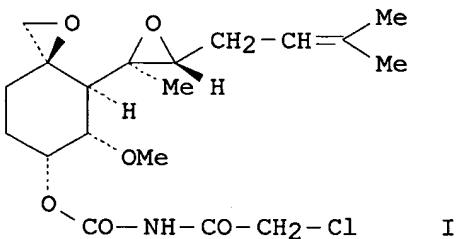
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:836837 CAPLUS
DN 139:328369
TI TNP-470 conjugates with HPMA copolymer as angiogenesis inhibitors
IN Satchi-Fainaro, Ronit; Folkman, Judah
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|---|----------|-----------------|----------|
| PI | WO 2003086382 | A1 | 20031023 | WO 2003-US10976 | 20030410 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, | | | |

| | | | |
|--|---|-----------------|----------|
| LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | |
| CA 2480666 | AA 20031023 | CA 2003-2480666 | 20030410 |
| AU 2003230852 | A1 20031027 | AU 2003-230852 | 20030410 |
| EP 1494662 | A1 20050112 | EP 2003-723958 | 20030410 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| US 2005169881 | A1 20050804 | US 2003-511009 | 20030410 |
| JP 2005529870 | T2 20051006 | JP 2003-583402 | 20030410 |
| US 2004229945 | A1 20041118 | US 2004-783986 | 20040219 |
| US 6949584 | B2 20050927 | | |
| US 2006020024 | A1 20060126 | US 2005-185538 | 20050720 |
| PRAI US 2002-371791P | P 20020411 | | |
| US 2002-414705P | P 20020930 | | |
| WO 2003-US10976 | W 20030410 | | |
| US 2004-783986 | A1 20040219 | | |

GI



AB The present invention relates to conjugates of water-soluble polymers and o-(chloracetylcarbamoyl)fumagillool (TNP-470) and use of those conjugates as specific intracellular carriers of the TNP-470 into tumor vessels. The present invention further relates to use of those conjugates to lower the neurotoxicity of TNP-470. Most preferably, the polymer has a mol. weight in the range of 15 kDa to 40 kDa. HPMA copolymer with methacryloyl-Gly-Phe-Leu-Gly p-nitrophenyl ester was prepared, aminolyzed with ethylene diamine and reacted with TNP-470 (I) to give the conjugate. The conjugate was tested for antitumor activity and angiogenesis inhibition in the Miles assay.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:836749 CAPLUS
DN 139:302515
TI Methods for treating edema-related diseases by modulating vascular hyperpermeability, angiogenesis and tight junctions
IN Soker, Shay; Satchi-Fainaro, Ronit
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English

10/511,009

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | WO 2003086178 | A2 | 20031023 | WO 2003-US11265 | 20030411 |
| | WO 2003086178 | A3 | 20040108 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2480809 | AA | 20031023 | CA 2003-2480809 | 20030411 |
| | AU 2003226349 | A1 | 20031027 | AU 2003-226349 | 20030411 |
| | EP 1494699 | A2 | 20050112 | EP 2003-746738 | 20030411 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2006506321 | T2 | 20060223 | JP 2003-583209 | 20030411 |
| | US 2005112063 | A1 | 20050526 | US 2004-962901 | 20041012 |
| | US 2005203013 | A1 | 20050915 | US 2004-962723 | 20041012 |
| PRAI | US 2002-371841P | P | 20020411 | | |
| | WO 2003-US11265 | W | 20030411 | | |
| AB | The present invention relates to methods for decreasing or inhibiting disorders associated with vascular hyperpermeability and to methods of screening for compds. that affect permeability, angiogenesis and stabilize tight junctions. In one aspect of the present invention there is provided a method of decreasing or inhibiting vascular hyperpermeability in an individual in need of such treatment. The method includes administering to the individual an effective amount of an antiangiogenic compound selected from the group consisting of endostatin, thrombospondin, angiostatin, tumstatin, arrestin, recombinant EPO and polymer conjugated TNP-470. Other antiangiogenic compds. are disclosed herein. | | | | |

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:750448 CAPLUS

DN 139:281208

TI Targeting of myocardial angiogenesis through CD13/APN conjugates and use for diagnosis and therapy of cardiovascular diseases

IN Demuinck, Ebo D.; Shapiro, Linda H.

PA Cardiovascular Research Institute Maastricht, Neth.; St. Jude Children's Research Hospital

SO Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DT Patent

LA English

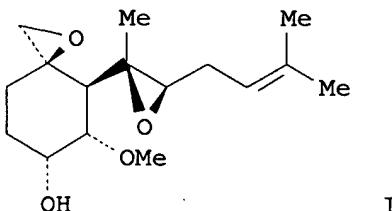
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | EP 1346729 | A1 | 20030924 | EP 2002-76146 | 20020319 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | WO 2003078569 | A2 | 20030925 | WO 2003-NL207 | 20030319 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, | | | | |

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003225405 Al 20030929 AU 2003-225405 20030319
 PRAI EP 2002-76146 A 20020319
 US 2002-365190P P 20020319
 WO 2003-NL207 W 20030319
 AB The present invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety for treating or diagnosing a cardiovascular disease. The invention further relates to methods in which these conjugates are used to target therapeutic agents or imaging mols. to the cardiovascular system. In particular the invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with angiogenesis-promoting factors for use in the treatment of ischemic myocardium or extremities. The invention also relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety that favorably alters wound healing after percutaneous arterial intervention. The invention further relates to conjugates comprising a CD13/APN homing mol. that is conjugated with a moiety that favorably alters atherosclerotic plaques, such as an angiogenesis inhibitor, for use in stabilizing or reducing the size of atherosclerotic plaques. Finally, the invention relates to conjugates comprising a CD13/APN homing mol. that is conjugated with an imaging moiety for use in diagnostic methods comprising vascular imaging.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2003:101908 CAPLUS
 DN 138:401909
 TI Concise stereocontrolled routes to fumagillol, fumagillin, and TNP-470
 AU Vosburg, David A.; Weiler, Sven; Sorensen, Erik J.
 CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
 SO Chirality (2003), 15(2), 156-166
 CODEN: CHRLEP; ISSN: 0899-0042
 PB Wiley-Liss, Inc.
 DT Journal
 LA English
 OS CASREACT 138:401909
 GI



AB A concise, diastereoselective synthesis of (\pm)-fumagillol (I) and formal, enantioselective syntheses of the potent angiogenesis inhibitors fumagillin and TNP-470 are reported. The origin of asymmetry is a highly diastereoselective Diels-Alder reaction using a

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diene with a chiral oxazolidinone auxiliary. The stereochem. course of a key conjugate addition reaction is controlled by the cup-shaped architecture of a cis-fused bicyclic enal. Other key steps include a facile hetero-Claisen rearrangement and a site-selective Sharpless epoxidn.

RE.CNT 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:935435 CAPLUS
DN 136:84677
TI Methods for enhancing antibody-induced cell lysis and treating cancer
IN Weiner, George; Hartmann, Gunther
PA University of Iowa Research Foundation, USA
SO PCT Int. Appl., 312 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2001097843 | A2 | 20011227 | WO 2001-US20154 | 20010622 |
| WO 2001097843 | A3 | 20030123 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2410371 | AA | 20011227 | CA 2001-2410371 | 20010622 |
| US 2003026801 | A1 | 20030206 | US 2001-888326 | 20010622 |
| EP 1296714 | A2 | 20030402 | EP 2001-948684 | 20010622 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003535907 | T2 | 20031202 | JP 2002-503327 | 20010622 |
| PRAI US 2000-213346P | P | 20000622 | | |
| WO 2001-US20154 | W | 20010622 | | |
| AB The invention relates to methods and products for treating cancer. In particular the invention relates to combinations of nucleic acids and antibodies for the treatment and prevention of cancer. The invention also relates to diagnostic methods for screening cancer cells. | | | | |

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:824135 CAPLUS
DN 134:21434
TI Enzyme-activated antitumor prodrug compounds
IN Firestone, Raymond A.; Telan, Leila A.
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000069472 | A2 | 20001123 | WO 2000-US10327 | 20000417 |
| WO 2000069472 | A3 | 20010531 | | |
| W: CA, JP, MX | | | | |

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE
 CA 2370245 AA 20001123 CA 2000-2370245 20000417
 EP 1181055 A2 20020227 EP 2000-923446 20000417
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI
 JP 2002544242 T2 20021224 JP 2000-617932 20000417
 PRAI US 1999-134135P P 19990514
 WO 2000-US10327 W 20000417
 AB Disclosed are enzyme-activated antitumor and antimetastatic prodrug
compds. The specific enzymes are collagenase(IV) and elastase. The
conjugate N-Cbz-Gly-Phe-Ala-Leu-doxorubicin was prepared and the
cleavage of this and other conjugates by enzymes was determined
 L5 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 1994:226788 CAPLUS
 DN 120:226788
 TI Drug delivery using biodegradable microspheres
 AU Okada, Hiroaki; Yamamoto, Masaki; Heya, Toshiro; Inoue, Yayoi; Kamei,
Shigeru; Ogawa, Yasuaki; Toguchi, Hajime
 CS DDS Res. Lab., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
 SO Journal of Controlled Release (1994), 28(1-3), 121-9
 CODEN: JCREEC; ISSN: 0168-3659
 DT Journal
 LA English
 AB Rational delivery systems for leuprorelin acetate, a potent LHRH agonist,
were achieved by developing a microsphere system using biodegradable
polymers, poly(lactic/glycolic acid) (PLGA) and poly(lactic acid), which
release the drug in a sustained-release fashion depending on the
biodegrdn. of polymer used and persistently suppress
steroidogenesis for over 1 and 3 mo, resp., following a single injection.
To produce these systems, the authors established a novel
microencapsulation technique, the in-water drying method, and microspheres
with a high trap ratio and small initial burst were obtained. A
microsphere system of TRH prepared using PLGA could also continuously
release the drug for 2 or 4 wk. Using these systems effectively reduced
the required dose compared with that needed with daily injection due to
more continuous receptor hits on the target organs and could improve
patient compliance. Chemoembolization using PLGA microspheres containing an
angiogenesis inhibitor, TNP-470, resulted in dramatic
regression of VX-2 carcinoma in rabbits. The microsphere system using
biodegradable polymers is useful in designing controlled release delivery
and targeted delivery to attain potent and rational therapy.

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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 57.25 | 57.46 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -12.75 | -12.75 |